IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF NORTH CAROLINA
WESTERN DIVISION

JIMMY EARP AND PATRICIA EARP, Plaintiffs, v. NOVARTIS PHARMACEUTICALS CORPORATION, Defendant.	**NOVARTIS PHARMACEUTICALS CORPORATION'S MEMORANDUM OF LAW IN SUPPORT OF OMNIBUS MOTION *IN LIMINE*** **Case No. 5:11-cv-00680-D**

Novartis Pharmaceuticals Corporation ("Novartis") submits this memorandum of law in support of its Omnibus Motion *in Limine*. The Court should exclude from trial evidence or argument regarding: (1) corporate conduct or knowledge that post-dates Mr. Earp's triggering tooth extractions in June 2001 or, in the alternative, his last infusion with a Novartis product in February 2002; (2) certain irrelevant "early warning" evidence that could not have put a drug manufacturer acting in the exercise of ordinary care on notice that Aredia or Zometa could cause osteonecrosis of the jaw ("ONJ"); (3) labeling and dosing issues controlled by the FDA; (4) warnings Novartis allegedly should have provided to anyone other than Mr. Earp's prescribing physicians; (5) medical costs for Mr. Earp's Aredia and Zometa infusions; (6) photographs of injuries in patients other than Mr. Earp; (7) sales and marketing materials that were neither seen nor relied upon by Mr. Earp's prescribing physicians; (8) statements by Mr. Earp that he would not have used Aredia or Zometa if he had been told about the risk of ONJ; (9) references to Reclast and other Novartis drugs which are not at issue in this case; and (10) evidence of adverse drug event ("ADE") reports that do not discuss the injury at issue in this case.

STATEMENT OF FACTS

Plaintiffs in this pharmaceutical products liability lawsuit allege that Novartis's intravenous infusion drugs Aredia, sold generically as "pamidronate," and Zometa caused Mr. Earp to develop

ONJ. The FDA approved Aredia (including its labeling) in 1995 as safe and effective for the treatment of multiple myeloma and later approved Zometa for the same use.[1] Oncologists prescribe Aredia and Zometa, which are in a class of drugs called bisphosphonates, to prevent or delay debilitating skeletal-related events in patients with multiple myeloma or with cancer that has spread to their bone. In April 2001, the FDA approved the marketing of a generic version of pamidronate, manufactured and sold by Bedford Laboratories, as a bioequivalent to Aredia.[2] The FDA subsequently approved additional generic pamidronate products manufactured and sold by other pharmaceutical companies.[3] The market share of Aredia dropped dramatically after the FDA approved generic pamidronate – to 35% for 2002, then to 7% for 2003, and then to 2% for 2004.[4] Aredia, the generic form pamidronate, and Zometa are still considered the standard of care for treating multiple myeloma patients.[5] Novartis received its first adverse event report regarding ONJ in a patient using Aredia or Zometa in December 2002.[6] Plaintiffs' expert, Dr. Robert Marx, has testified that ONJ was an "unknown" entity in August 2003 and that he was the first to publish about ONJ in bisphosphonate users in September 2003.[7] That same month, Novartis revised its Aredia and Zometa labeling to include reports of ONJ.[8] Plaintiff Jimmy Earp's transplant oncologist, Dr. Alan Kritz, first prescribed Aredia for him in March 1998 because "Aredia decreased skeletal events in patients with myeloma" and, because Mr. Earp "certainly . . . was at risk for further skeletal events

[1] *See* 9/1/1995 FDA Approval Letter (ZA-0858220-221) (Ex. 1); 2/22/2002 FDA Approval Letter (ZA-0706772-774) (Ex.2).

[2] *See* 9/12/2007 Affidavit of Emily Chee ("Chee Aff.") ¶¶ C-D (redacted version, Ex. 3).

[3] *Id*.

[4] *Id.*

[5] *See* Dep. Tr. of Mark Yoffe, MD ("Yoffe Dep.") at 67 (Ex.4).

[6] *See* DCT Adverse Event Summary Form (Dec. 6, 2002) (ADE-0023162-164) (Ex. 5).

[7] 5/15/2007 Dep. Tr. of Dr. Robert Marx at 169, 190, 309 (Ex. 6).

[8] *See* 9/26/2003 Sterner Letter to Orloff (ZNDA-0108101) (Ex.7).

going forward."[9] In April 1999 Mr. Earp's tooth #19 was extracted and in June 2001 his teeth #s 30 & 31 were extracted, allegedly triggering his subsequent jaw problems.[10] Mr. Earp's oncologist, Dr. Mark Yoffe, continued to treat him with Aredia until he switched Mr. Earp to Zometa in November 2001 because of its "short infusion."[11] Mr. Earp's last Zometa infusion was on February 14, 2002.[12] Dr. Yoffe halted Mr. Earp's Zometa therapy in March 2002 because he experienced renal insufficiency.[13] Dr. Yoffe subsequently prescribed pamidronate therapy to Mr. Earp from April 8, 2002 to January 12, 2004.[14] Dr. Yoffe testified that, although the medical records reflect that he prescribed "Aredia," he used the term "Aredia" interchangeably with generic pamidronate and he could not say whether Mr. Earp actually received Novartis's product Aredia or generic pamidronate.[15]

ARGUMENT

I. Corporate Conduct or Knowledge Evidence that Post-Dates Mr. Earp's Triggering Tooth Extractions in June 2001 Or, In the Alternative, His Last Infusion With A Novartis Product In February 2002 Should Be Excluded Under Rules 401, 403, and 407.

The Court should exclude evidence or argument about Novartis's corporate conduct or knowledge of the purported risk of ONJ as a side effect of Aredia or Zometa therapy that post-dates plaintiff Jimmy Earp's tooth extractions in June 2001, which, along with an earlier extraction in April

[9] 1/20/2011 Dep. Tr. of Dr. Alan D. Kritz ("Kritz Dep.") at 60 (Ex.8); *see also* Health Care Record of 3/13/1998 (6757-1187) (Ex. 9). The parties have agreed that it is not necessary to file the attached medical records under seal (provided that Mr. Earp's date of birth and social security number are redacted) because these unsealed medical records were previously filed in the United States District Court for the Middle District of Tennessee.

[10] *See* 2/16/2011 Expert Report of Dr. Frederick L. Nance at 2 (Ex. 10).

[11] *See* Health Care Record of 11/16/2001 (6757-0606-0607) (Ex.11).

[12] *See* Health Care Record of 2/14/2002 (6757-1677) (Ex. 12).

[13] *See* Yoffe Dep. at 85.

[14] *See id.*

[15] *Id.* at 89-91 ("Q. So would you sometimes write Aredia where the patient was receiving Pamidronate? A. Yes. … Q. And do you know what the infusion center where Mr. Earp would get his infusion stocks, whether it's generic Aredia or Aredia itself? A. No.").

1999, allegedly triggered his jaw problems.[16] Evidence of Novartis's conduct or knowledge that post-dates this triggering event is not relevant, and any nominal relevance is substantially outweighed by the potential to mislead and confuse the jury and unfairly prejudice Novartis.[17]

Even if the Court does not agree that corporate conduct evidence post-dating the injury-triggering event is excludable, this evidence is certainly precluded after Mr. Earp's last use of the Novartis products he claims caused his injury (February 14, 2002).[18] Corporate conduct occurring after that date, February 2002, cannot make more or less probable the central question in this case: whether an inadequate warning by Novartis regarding its drugs Aredia and Zometa proximately caused Mr. Earp to develop ONJ.[19] Evidence post-dating plaintiff's last use of Novartis's drugs is inadmissible because it is irrelevant, Fed. R. Evid. 401-02, is unfairly prejudicial and confusing, Fed. R. Evid. 403, and is evidence of Novartis's subsequent remedial measures, Fed. R. Evid. 407.

"A fundamental principle of traditional product liability law is that the plaintiff must prove that the defendant supplied the product which caused the injury."[20] In a products liability action

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[16] These extractions were necessary and unavoidable, and therefore plaintiffs cannot meet their burden of proof on warnings causation in this case. *See, e.g., Zimmerman v. Novartis Pharm. Corp.*, 287 F.R.D. 357, 361 (D. Md. 2012) (granting summary judgment because "Defendant has provided uncontroverted evidence demonstrating that even if Defendant had warned of the risk of ONJ in Aredia/Zometa patients," plaintiff's dental treatment would not have changed); *Eberhart v. Novartis Pharms Corp.*, 867 F. Supp. 2d 1241, 1255-56 (N.D. Ga. 2011) (granting summary judgment where plaintiff could not show that an adequate warning would have prevented alleged ONJ).

[17] Fed. R. Evid. 401-03.

[18] *See* Pls.' Position, Jt. Status Rpt., D.E. 103, at 3 (asserting that "almost every Court" in the Aredia/Zometa litigation has cut off corporate conduct evidence after "the last infusion of Zometa."); *see also* Order at 10-11, *Fussman v. Novartis Pharm. Corp.*, No. 1:06-cv-149, (M.D.N.C. Oct. 29, 2010) (limiting evidence of Novartis's actions after plaintiff stopped receiving Zometa because it "would not be directly relevant to the adequacy of the warnings in this case") (Ex.13).

[19] *See* N.C. Stat. Ann. § 99B-5(a) (West).

[20] *See In re Aredia & Zometa Products Liab. Litig.*, 3:06-MD-1760, 2007 WL 4387376, at *2 (M.D. Tenn. Nov. 30, 2007) (Ex. 69); *see also Lee v. Baxter Healthcare Corp.*, 721 F. Supp. 89, 92 (D. Md. 1989) (under products liability law, "the plaintiff must prove that the defendant manufacturer made the product that caused plaintiff's injury."), *aff'd sub nom. Lee v. Baxter Health Care Corp.*, 898 F.2d 146 (4th Cir. 1990).

under North Carolina law, "Plaintiff must establish each essential element of the case."[21] This includes providing "evidence which tends to show that *the product manufactured by defendant* was defective . ..."[22] In recognition of this principle, and understanding the diminished market share of Novartis's Aredia post-2001, the Multidistrict Litigation Court instructed plaintiffs in the Aredia/Zometa litigation to provide a "Product Identification Submission" that "detail[ed] with specificity the efforts made to obtain" an affidavit or declaration "from the pharmacy manager or similarly-situated person at each infusion center where that plaintiff allegedly received Aredia® infusions to establish, based on that infusion center's records, which infusions received by that plaintiff were name-brand Aredia®, as opposed to generic pamidronate disodium."[23] Plaintiffs failed to satisfy the burden under North Carolina law or under the MDL Order requiring them to establish Mr. Earp's use of name-brand Aredia, particularly during the period 2002 – 2004 when generic pamidronate occupied the vast majority of the market.[24]

The only evidence in this case regarding product identification is the testimony of Mr. Earp's prescribing oncologist, who could not say whether Mr. Earp was infused with brand Aredia or generic pamidronate at any time.[25] It is clear, however, that when Mr. Earp was switched back to pamidronate from Zometa, name brand Aredia's market share was steadily dwindling down to a mere

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[21] *Hensley v. Danek Med., Inc.*, 32 F. Supp. 2d 345, 351 (W.D.N.C. 1998) (citing *Celotex Corp. v. Catrett*, 477 U.S. 317, 323–24 (1986)).

[22] *Jolley v. Gen. Motors Corp.*, 55 N.C. App. 383, 385-86, 285 S.E.2d 301, 303 (1982) (emphasis added); *see also Couick v. Wyeth, Inc.*, 691 F. Supp. 2d 643, 646 (W.D.N.C. 2010) (name-brand drug manufacturer not liable for failure to warn under North Carolina law for injuries caused by generic drug).

[23] Agreed Order ¶ 4, *In re Aredia & Zometa Products Liab. Litig.*, 3:06-MD-1760 (M.D. Tenn. Jan. 14, 2008) (Ex. 14).

[24] Novartis argued in its motion for summary judgment that plaintiffs could not meet their burden to prove that Mr. Earp was infused with name-brand Aredia after April 2001. *See* Novartis' Mem. in Support of Mot. for Summ. J. at 4 n. 2, D.E. 79. Plaintiffs did not respond and therefore conceded they have failed to establish Aredia use after April 2001. *See, generally,* Pls.' Opp. to Def.'s Second Mot. for Summ. J., D.E. 81.

[25] *See* Yoffe Dep. at 89-91.

fraction.[26] It is plaintiffs' burden to establish that Mr. Earp received Novartis's Aredia at a time when another pharmaceutical company marketing generic pamidronate held 93% of the market.[27] They have offered nothing to support the highly improbable likelihood that Mr. Earp used a Novartis product after February 2002 and waived any such argument by not raising it in response to Novartis's Motion for Summary Judgment.[28]

Because plaintiffs have failed to establish that Mr. Earp was treated with a Novartis product after his last infusion of Zometa in February 2002, the Court should exclude any evidence or argument referring to events that occurred after that date pursuant to Federal Rules of Evidence 401-403.[29] Evidence that post-dates February 14, 2002 is not evidence of notice or of Novartis's state of mind at a time when it could have made a difference to the alleged injury in this case. As this Court has held, such after-the-fact evidence "is confusing, potentially misleading, and a waste of time" and "[t]hese considerations substantially outweigh any probative value of the evidence."[30] Moreover, evidence relating to label changes, notice issues, or other corporate conduct that post-date Mr. Earp's last infusion of a Novartis drug is inadmissible as a subsequent remedial measure.[31] This Court and

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[26] *See* Chee Aff.

[27] Self-serving statements by Mr. Earp and billing records listing "Aredia" are not enough to overcome plaintiffs' burden.

[28] *See Dore v. Novartis Pharm. Corp.*, No. 06-2271, Op. at 9-10 (D.N.J. Jun. 7, 2012) (granting partial summary judgment for Novartis in Aredia/Zometa case in relation to infusions plaintiff could not prove were Novartis's drug) (Ex. 15).

[29] *See Jimenez v. DaimlerChrysler Corp.*, 269 F.3d 439, 451-52 (4th Cir. 2001) (finding evidence of post-design discovery of a problem did not support a punitive damages claim); *In re Fosamax Prods. Liab. Litig.*, 06-MD-1789, Hr'g Tr. at 481:8-13 (S.D.N.Y. July 29, 2009) ("[A]ny evidence of Merck's conduct after September of 2003 is inadmissible if offered to show what Merck knew or should have known about the risks of ONJ after that date or to show the inadequacy of the warnings given after that date. Merck's failure to warn after it became too late to save the plaintiff's jaw is irrelevant to the claims in this case.") (Ex. 16).

[30] *Silicon Knights, Inc. v. Epic Games, Inc.*, 5:07-CV-275-D, 2011 WL 5439156, at *3 (E.D.N.C. Nov. 8, 2011) (excluding evidence under Fed. R. Evid. 403) (Ex. 72).

[31] Fed. R. Evid. 407; *see also, e.g., Werner v. Upjohn Co., Inc.*, 628 F.2d 848, 854 (4th Cir. 1980) (holding use of evidence of subsequent remedial measures to argue negligence by drug company "is strictly forbidden by the policy-based Rule 407"), *cert. denied*, 449 U.S. 1080 (1981); *Krasnopolsky v.*

other courts presiding over Aredia/Zometa cases also have excluded evidence post-dating the plaintiffs' last infusions as subsequent remedial measures precluded by Rule 407.[32] This Court should likewise apply Rule 407 to exclude evidence of Novartis's conduct and knowledge it gained only after Mr. Earp's last Zometa infusion on February 14, 2002.[33]

The following documents, which plaintiffs likely will seek to offer in their case, all post-date Mr. Earp's last infusion with a Novartis drug and therefore are irrelevant and unduly prejudicial. They are also inadmissible for the additional reasons that follow.

1. October 21, 2005 e-mail from Eric Slosberg titled "AAOMS ONJ Survey" (ZA-0803454, ZAEM-001484228-29) (combined as Ex. 19). This e-mail chain discusses a conversation that Dr. Regina Landesberg (an independent physician) purportedly had with Eric Slosberg (a Novartis employee). In the chain, Mr. Slosberg writes:

> Dr Regina Landesberg (Columbia University) informed me about some activities that the American Association of Oral and Maxillofacial Surgeons (AAOMS) is planning. She implored to me that this must remain confidential, that the committee should

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Warner-Lambert Co., 799 F. Supp. 1342, 1348 (E.D.N.Y. 1992) (excluding evidence of pharmaceutical company's "further testing and/or investigation of Meclomen" after plaintiff's treatment with the drug).

[32] *See Brown v. Novartis Pharm. Corp.*, No. 7:08-CV-130-FL, 2012 WL 3066588, at *14 (E.D.N.C. July 27, 2012) (excluding evidence of the 2007 and 2008 labeling changes for Zometa and Aredia under Rule 407); Order at 2, *Brodie v. Novartis Pharm. Corp.*, No. 4:10CV138 HEA (E.D. Mo. Jan. 9, 2012) (same) (Ex. 17); *Mahaney ex. rel. Estate of Kyle v. Novartis Pharm. Corp.*, 835 F. Supp. 2d 299, 314 (W.D. Ky. 2011) (same); *Hogan v. Novartis Pharm. Corp.*, No. 06 CIV. 0260 BMC RER, 2011 WL 1336566, at *2-4 (E.D.N.Y. Apr. 6, 2011) (same) (Ex. 68); *see also* Trial Tr. at 1856-57, *Davids v. Novartis Pharm. Corp.*, No. CV-06-0431 (ADS) (E.D.N.Y. Oct. 22, 2012) ("*Davids* 10/22/12 Tr.") (excluding internal emails that post-dated plaintiff's last infusion as subsequent remedial measures) (Ex. 18).

[33] Plaintiffs likely will point to the Fourth Circuit's ruling upholding the *Fussman* court's trial-specific reversal of its initial decision to exclude evidence of the 2007 label change under Rule 407. *See Fussman v. Novartis Pharm. Corp.*, 509 F. App'x 215, 222 (4th Cir. 2013). The Fourth Circuit did not hold that the district court rightly allowed evidence of the label change, but only determined, under a post-trial standard, that they could not "conclude that" its admission "'substantially swayed' the jury's verdict." *Id.* By contrast, the Eastern District of North Carolina in *Brown* and numerous other Aredia/Zometa courts have concluded, under an evidentiary standard, that evidence of the 2007 and 2008 label changes should be barred. And, in a ruling affirmed by the Fourth Circuit, the *Fussman* trial court agreed that plaintiff could present evidence of Novartis's conduct only "during the time period while [plaintiff] continued to receive the Aredia and Zometa." *Fussman v. Novartis Pharm. Corp.*, 1:06CV149, 2011 WL 5836928, at *5 (M.D.N.C. Nov. 21, 2011), *aff'd*, 509 F. App'x 215 (4th Cir. 2013), *cert. denied*, 134 S. Ct. 88 (U.S. 2013) (Ex. 66).

> never find out that she informed Novartis about this. I trust that you will keep it so . . .

Plaintiffs will likely use this to suggest that Novartis acted improperly by using physicians to provide "secret information" concerning ONJ to Novartis.[34]

This email contains three levels of hearsay inadmissible under Rules 802 and 805. Mr. Slosberg's statements are not Novartis admissions because he had no authority to make them, and his statements relate other hearsay by Dr. Landesberg, who was neither a Novartis employee nor authorized to make statements on Novartis's behalf.[35] Dr. Landesberg's statements relay yet *other* out-of-court statements by members of the AAOMS. The e-mail chain is inadmissible triple hearsay as well as irrelevant.

2. June 14, 2005 and June 15, 2005 e-mails from Katarzyna Sablinska (ZAEM-02131140-44) (Ex. 21). In these e-mails, Dr. Sablinska, a Novartis epidemiologist, disagreed that certain other risk factors for ONJ in a draft press release were "well-documented." Plaintiffs will argue that this proves that the FDA-approved Zometa label was false and misleading when it described these risk factors as "well-documented."[36]

Dr. Sablinska's e-mails should be excluded under Rules 401-03, because they are irrelevant, and, if relevant, any probative value is outweighed by the risk of unfair prejudice to Novartis. The Zometa labels that describe other risk factors for ONJ were distributed to prescribing physicians in December 2003, well after the extractions that allegedly triggered Mr. Earp's jaw problem and nearly

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[34] *See* 1/25/2012 Trial Tr. at 66-67, *Kyle-Mahaney v. Novartis Pharm. Corp.*, No. 1:06-CV-00035 (W.D. Ky.) (Ex. 20).

[35] *See* Fed. R. Evid. 801(d)(2) (not party admission unless the statement was made "by a person whom the party authorized to make a statement on the subject" or "by the party's agent or employee on a matter within the scope of that relationship"); *see also Precision Piping & Instruments, Inc. v. E.I. du Pont de Nemours & Co.*, 951 F.2d 613, 619-20 (4th Cir. 1991) (excluding statements regarding contracts as hearsay absent evidence speaker had authority to hire or fire workers, and because the "remarks were not made within the scope of his employment").

[36] *See Davids* 10/22/12 Tr. at 1860.

two years after his last infusion with Zometa. Nothing in the subsequent labeling could have contributed to his jaw injury.

3. March 16, 2005 Advisory Panel Recommendations Concerning Reclast (ZAEM-00391915-21) (Ex. 23). In this document, the "Zoledronic Acid Bone Clinical Development Group" panel was discussing the development of what became Reclast, *i.e.*, zoledronic acid for benign indications, not cancer. The participants discussed how the label for Reclast should differ from the label of Zometa on the listing of other risk factors for ONJ. Although the two different drugs share the same active ingredient, the conditions for which they are prescribed are very different: cancer patients given Zometa receive a plethora of other drugs – chemotherapy, steroids, thalidomide, etc. – that are uncommon in patients receiving Reclast. Accordingly, the recommendations for the Reclast label are irrelevant to the adequacy of the Zometa label and under Rule 401 and 403 are irrelevant or otherwise would be misleading and cause confusion and unfair prejudice.[37]

4. June 25, 2004 e-mail from former Novartis employee Linda Weiss (ZAEM-01606488) (Ex. 26). In this e-mail, Dr. Weiss, a former Novartis medical information specialist, speculated on a possible alternative dosage of Zometa, commenting that, in her view, a 2 mg dose of Zometa was as effective as the FDA-approved 4 mg dose. It is undisputed that Dr. Weiss was not part of the clinical research program that developed the FDA-approved 4 mg dose and that it was not within Dr. Weiss's job description to address potential modifications to FDA-approved doses. Dr. Weiss had neither the expertise nor the corporate authority to make the statement at issue.[38]

The issue of a 2 mg dose versus a 4 mg dose is also irrelevant to any issue in this case. No expert witness has been identified by plaintiffs to testify – or who *can* testify – that, had Mr. Earp

[37] *See Kyle*, 835 F. Supp. 2d at 314 (excluding document "[t]o protect against confusion between these two drugs").

[38] *See Precision Piping & Instruments, Inc.*, 951 F.2d at 619-20; *see also Aliotta v. Nat'l R.R. Passenger Corp.*, 315 F. 3d 756, 763 (7th Cir. 2003) (party admissions "properly excluded" under Rules 701(c) and 702 when they contained "unqualified and unreliable scientific knowledge").

been given Zometa at 2 mg instead of 4 mg, he would not have developed ONJ or that his ONJ would otherwise have been materially different.[39] In fact, his precipitating extractions occurred *before* he had his first dose of Zometa (in November 2001).

5. May 2004 and later e-mails from outside advisors about draft "White Paper." These e-mails include criticisms of portions of draft ONJ treatment guidelines known as the "White Paper," which was developed by a panel of outside advisors and thereafter distributed by Novartis.[40] These e-mails suggest edits to a *draft* White Paper, not the final version. In prior trials, plaintiffs have sought to introduce portions of these out-of-court criticisms, such as the suggestion by a Dr. Schubert that listing other risk factors for ONJ was akin to "blowing smoke" and his advice that Novartis "take a bold and honest approach" by not discussing such risk factors.[41] Rules 801-02 bar the admission of these hearsay statements because none of the authors of these comments was an employee, agent, or representative of Novartis, nor is there any evidence suggesting that these independent practitioners were authorized to make such statements on Novartis's behalf.[42]

In this case, Mr. Earp had ceased his Zometa – and bisphosphonate – treatment long before the 2004 emails in question, so these e-mails are irrelevant under Rule 401 and any probative value they have is significantly outweighed by the risk of jury confusion and prejudice to Novartis under Rule 403.

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[39] Any suggestion that a 2 mg dose would be as effective as a 4 mg dose is preempted. *See infra* Part III.

[40] *See, e.g.*, ZAEM-00860680-81; ZAEM-00860748-49; ZAEM-00217697-700 (combined as Ex. 28).

[41] *See* 11/18/2010 Pl.'s Closing Statements at 11-13, *Fussman v. Novartis Pharm. Corp.*, No. 1:06-cv-00149 (M.D.N.C.) ("*Fussman* Closing Statements").

[42] *See, e.g.*, *Womack v. Tierco Maryland Inc.*, 38 F. App'x 850, 857 (4th Cir. 2002) (holding district court erred by not excluding out-of-court statements of independent vendor as hearsay absent evidence the "vendor was an agent or employee of [defendant] or that the statements concerned matters within the scope of his agency or employment"); *Brown v. Novartis Pharm. Corp.*, No. 7:08-CV-130-FL, 2012 WL 3066588, at *12-13 (E.D.N.C. July 27, 2012) (excluding emails). In *Fussman*, the Fourth Circuit merely applied an abuse of discretion, as opposed to an evidentiary, standard in holding that, even if the "White Paper" advisor emails were inadmissible hearsay, any error did not justify a new trial. *See Fussman*, 509 F. App'x at 219. In addition, the plaintiff was still taking Zometa, a Novartis drug, through June 2005. *Id.* at 217.

6. March 12, 2004 e-mail from Linda Weiss (ZAEM-00824590) (Ex. 29). Here, Dr. Weiss discusses the number of ONJ cases reported to Novartis and suggests that she "would be extremely cautious about using numbers [of case reports] with any of our customers" and that Novartis should "implicate the risk factors as much as possible e.g. radiotherapy, chemotherapy, dental procedures, etc." which were set forth in the FDA-approved label then in effect when conferring with prescribing oncologists. Plaintiffs likely will use this e-mail to improperly imply that Novartis hid information about the number of ONJ case reports from oncologists. The e-mail is not relevant to this case, because there is no evidence that any Novartis sales representative "implicated the risk factors" in discussions with Drs. Kritz or Yoffe – or with any other oncologist – or, in any event, that any "implication of risk factors" affected those physicians' prescribing decisions regarding Mr. Earp, which occurred years before this e-mail. Even if it were relevant, any probative value is far outweighed by the potential to mislead the jury and unfairly prejudice Novartis.[43]

7. January 18, 2004 fax from sales representative Samuel Klein (ZA-0525027/ZA-0466205) (combined as Ex. 30). Mr. Klein, a former Novartis sales representative, sent to Dr. Deborah Dunsire, another Novartis employee, a fax stating: "I have enclosed some internet postings regarding ONJ. Some of this is quite interesting and may even help identify potential 'enemies and allies.'" Plaintiffs may argue that this letter establishes that Novartis considered an "enemy" anyone who connected ONJ with Zometa. This out-of-court statement is inadmissible under Rules 801-02. Mr. Klein was not a Novartis decision-maker but a sales representative, was not authorized to make statements on this subject and, therefore, was addressing a matter outside the scope of his employment.[44] This unauthorized hearsay should also be excluded under Rules 401-03, because it is

[43] Fed. R. Evid. 401-03.

[44] *See* 8/7/2009 Dep. of Samuel Klein at 260, *Kelly v. Novartis Pharm. Corp.*, MID-L-2370-08-MT (N.J. Super. Ct. Law Div.) (explaining he did not typically write such letters) (Ex. 31); *see also* 11/10/2010 Trial Tr. at 89, *Fussman v. Novartis Pharm. Corp.*, No. 1:06-cv-149 (M.D.N.C.) (excluding 1/18/2004 Klein fax as hearsay) (Ex. 32).

irrelevant, and, even if relevant, any probative value is substantially outweighed by the potential unfair prejudicial effect on the jury.

8. December 1, 2003 e-mail from Margaret Linguri (ZAEM-01199529-32) (Ex. 27). Ms. Linguri, a Zometa Brand Team Leader, prepared a draft agenda for Novartis's December 2003 Advisory Board, a Novartis meeting bringing together outside oncologists and oral surgeons to elicit views on ONJ in patients treated with bisphosphonates. The objectives listed on the draft include "[g]ain[ing] agreement that osteonecrosis of the jaw pre-existed bisphosphonates and can be caused by a multitude of factors in patients with and without cancer." Plaintiffs will contend that this draft constituted a "secret" agenda and will argue that the Advisory Board process was illegitimate because the final agenda did not contain the above quoted objective. Both the draft agenda *and* final agendas are irrelevant to any issue in this case, and any probative value is far outweighed by the potential prejudice to Novartis.[45]

9. June 20, 2003 and July 10, 2003 e-mails from former Novartis employee Dr. Carsten Goessl (ZAEM-00133003) (Ex. 33) and (ZAEM-00077111) (Ex. 34). In the June 20, 2003 email, Dr. Goessl (a former clinical research physician for Novartis) hypothesized about potential mechanisms for the newly reported ONJ cases in Aredia and Zometa users, noting case reports about oral manifestations of osteopetrosis, a genetic bone disease. The e-mail expressed his belief that there was a "possible" but unproven "link" between intravenous bisphosphonates and "orofacial osteonecrosis." In the July 10, 2003 e-mail, Dr. Goessl, who was continuing to investigate ONJ, summarized articles discussing jaw abnormalities and noted that in one there was no reference to "chemotherapy-induced jaw/facial [osteonecrosis]." Plaintiffs likely will allege that these e-mails should have put Novartis on notice that bisphosphonates might be associated with ONJ. In fact,

[45] Fed. R. Evid. 401-03; *see also Precision Piping & Instruments, Inc.*, 951 F.2d at 620 (even if statement meets hearsay exception, it is inadmissible when it is "so unreliable that its probative value is substantially outweighed by the danger of prejudice and confusion") (citations omitted).

Novartis was already investigating reports of ONJ in patients on its drugs as of January 2003. One researcher's speculative hypotheses during the course of an investigation are irrelevant, and even if relevant, would have the potential to mislead and confuse the jury, and therefore should be excluded under Rules 401-03.

10. May 5, 2003 e-mail from Novartis employee Stefano Fratarcangeli (ZAED-00079439-43) (Ex. 35). Mr. Fratarcangeli discussed Novartis's planned response to initial reports of ONJ in cancer patients receiving bisphosphonates, including those that might be presented in an article intended to be written by a Dr. Ruggiero. The email states in part "we'll try to avoid that the paper is ever published" and "[t]his could turn into a 'snow ball' effect with potentially some news noise." Plaintiff will attempt to use the email to speculate that Novartis *actually* initiated efforts to prevent the publication of this article.[46] Not only is this e-mail the comments of a single employee, but they are speculative words, not conduct. As Judge Rakoff noted in the *Hill* Aredia/Zometa case when dismissing corporate documents as evidence supporting punitive damages, ostensibly bad thoughts are not sufficient evidence; they have to be "coupled" with bad corporate acts.[47] There is no evidence that any of these speculative words ever were acted upon, and therefore the e-mail is clearly irrelevant. Even if relevant, the e-mail invites confusion and could lead the jury to unfairly prejudicing Novartis.[48]

11. January 29, 2003 e-mail from David Epstein (NJZAEM-00047909-47) (Ex. 39). In this e-mail, Mr. Epstein, chief executive officer of Novartis's oncology business, discusses a

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[46] *See* 11/1/2012 Pl.'s Closing Statements at 2857, *Davids v. Novartis Pharm. Corp.*, No. 2:06-cv-0431 (E.D.N.Y) ("*Davids* 11/1/12 Tr.") (Ex. 36). In fact, Dr. Ruggiero *did* publish his article. *See* Ruggiero, et al., *Osteonecrosis of the Jaws Associated With the Use of Bisphosphonates: A Review of 63 Cases*, 62 J. ORAL MAXILLOFAC. SURG. 527 (2004) (Ex. 37). Dr. Ruggiero could not say that Novartis had done anything to prevent publication. *See* 5/12/2008 Dep. of Salvatore Ruggiero, D.M.D., M.D. at 47-48, *In re Aredia® & Zometa® Prods. Liab. Litig.*, No. 3:06-MD-1760 (M.D. Tenn.) (Ex. 38).

[47] Trial Tr. at 1092-93, *Hill v. Novartis Pharm. Corp.*, No. 1:06-cv-00939-JSR-SAB (E.D. Cal. June 18, 2013) (Ex. 73).

[48] Fed. R. Evid. 401-03; *see also Precision Piping & Instruments, Inc.*, 951 F.2d at 620.

Japanese study involving dosing regimens of zoledronic acid to treat medical conditions other than cancer, *i.e.*, Paget's disease and osteoporosis. He states that a "2mg dose in Japan runs the risk that physicians start to use 2mg in Malignant disease cutting our revenue in half. If that dose was to bleed into other markets, the global impact on sales could be very large." Plaintiffs will attempt to argue that Novartis was more concerned about profits than safety.[49] However, the email has nothing to do with ONJ and predates Mr. Epstein's knowledge of this potential adverse event.[50] Further, the Japanese study at issue does not involve patients with multiple myeloma or any other type of cancer.[51] Nor is there any admissible evidence that a 2 mg dose of Zometa would be as effective in fighting the devastating effects of multiple myeloma as the FDA-approved 4 mg dose. The Court should exclude this email under Rules 401-03.

II. Evidence or Argument Concerning Certain "Early Warning" Evidence Should Be Excluded as Irrelevant and Inadmissible Under Rules 401, 402, and 403.

Novartis received its first adverse drug event report regarding ONJ in bisphosphonate users in December 2002, nearly a year after Mr. Earp last used a Novartis drug. The first published report about ONJ in bisphosphonate users was in September 2003, the same month that Novartis first included reports of ONJ in the Aredia and Zometa labels. Yet plaintiffs will attempt to argue that Novartis should have known about ONJ prior to Mr. Earp's first infusion with Aredia in March 1998 because of: (a) the Gotcher & Jee rice rat study of a different drug, (b) "phossy jaw," a 19th-century industrial disease in match workers exposed to elemental phosphorus fumes, (c) the unrelated genetic disease osteopetrosis, and (d) potential cases of ONJ identified retrospectively in clinical trials patients. Plaintiffs cannot show that any of these things should have put a drug manufacturer acting

[49] *See, e.g.*, *Fussman* Closing Statements at 20-21 ("Can't use the lower dose. It might cut our revenues in half. . . . . That's Aredia and Zometa . . . . All about money.").

[50] *See* 2/9/2010 Dep. of David Epstein at 41, *In re Aredia® & Zometa® Prods. Liab. Litig.*, No. 278 MT (N.J. Super. Ct. Law Div.) (Ex. 40).

[51] *Id.* at 255-56.

in the exercise of ordinary care on notice that Aredia or Zometa could cause ONJ.[52] As a federal court recently held when granting Novartis summary judgment in an Aredia/Zometa case:

> Plaintiffs have not pointed to any evidence, including any testimony, suggesting that based on one study and six possible cases of ONJ in a clinical trial, Defendant's actions fell below the acceptable standard of care, i.e., what a reasonably prudent manufacturer would have known and warned about. Likewise, Plaintiffs have not pointed to any evidence or testimony that, in light of this article and six possible cases of ONJ in the clinical trial, ONJ was a knowable risk of using Aredia® in light of the generally recognized and prevailing best scientific and medical knowledge available at the time of manufacture and distribution.[53]

This "early warning" evidence should be excluded under Rules 401-03 as it is, among other things, irrelevant and its admission will unfairly prejudice Novartis and mislead and confuse the jury.[54]

A. The Gotcher & Jee rice rat study of a different drug is irrelevant.

Gotcher & Jee was a 1981 report about an experiment in rice rats (a species bred as a model to study periodontal disease) in which the drug clodronate was tested to see if it would reduce bone loss, which it did.[55] An unknown number of treated rats showed areas of "devitalized" bone, an observation that the study's authors did not characterize as an adverse effect of the drug.[56]

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[52] *See* N.C. Stat. Ann. §99B-5(a).

[53] *D'Agnese v. Novartis Pharm. Corp.*, 952 F. Supp. 2d 880, 891-92 (D. Ariz. 2013).

[54] This evidence and any testimony regarding it also should be excluded under Rule 702 because plaintiffs have no expert who can tie it to this case. *See Phillip v. GEO Grp., Inc.*, No. 5:09-CT-3115-FL, 2012 WL 5392120, at *6 (E.D.N.C. Nov. 5, 2012) ("[i]n cases involving 'complicated medical questions far removed from the ordinary experience and knowledge of laymen, only an expert can give competent opinion evidence as to the cause of an injury.'") (Ex. 71), *aff'd*, 520 F. App'x 215 (4th Cir. 2013). Dr. Marx – plaintiffs' only expert whose report offers an opinion on how bisphosphonates affect bone – "can't say that the Gotcher study is even a reliable indicator or a reliable model for testing for osteonecrosis of the jaw with bisphosphonates." 3/21/2012 Trial Tr. at 252, *Baldwin v. Novartis Pharm. Corp.*, No. 06-4049-CV-C-MJW (W.D. Mo.) (Ex. 44). Likewise, plaintiffs in the Aredia/Zometa litigation initially named Paul Hanson, Ph.D., a chemist, for the purpose of tying together "phossy jaw" and ONJ, but the judge overseeing the New Jersey mass tort litigation excluded his testimony as not scientifically reliable, and plaintiffs have failed to put forward any substitute. *See also* 9/11/13 Order at 6 (precluding Dr. Parisian from discussing issues other than "the FDA drug-approval process").

[55] *See* J.E. Gotcher & W.S.S. Jee, *The progress of the periodontal syndrome in the rice rat II: The effects of diphosphonate on the periodontum*, 1981 J. PERIODONTAL RES. 16(4): 441-55 (Ex. 41).

[56] *Id.* at 448, 452.

The study is irrelevant because it did not involve Aredia or Zometa, the drugs at issue in this case, but clodronate, a completely different bisphosphonate drug. Clodronate is a non-nitrogen containing bisphosphonate (unlike Aredia and Zometa),[57] and Dr. Marx – plaintiffs' main expert on general medical causation – is "a hundred percent" sure that ONJ is caused "*only* by nitrogen-containing bisphosphonates."[58] Plaintiffs have no evidence to establish that the study is relevant here.[59] Because any probative value is substantially outweighed by significant risks that the jury will be confused and misled and that Novartis will be unfairly prejudiced, it also should be excluded under Rule 403.[60]

B. The industrial illness "phossy jaw" cannot be tied to ONJ and is irrelevant.

"Phossy jaw" refers to a 19th-century malady in match-factory workers then thought to be associated with exposure to elemental phosphorus. Plaintiffs claim that because Aredia and Zometa contain phosphorus, and because "phossy jaw" might be similar to what is known as ONJ today, Novartis should have known that Aredia or Zometa could cause ONJ. Evidence relating to "phossy

[57] *See, e.g.*, Recenti et al., *Clodronate Acts on Human Osteoclastic Cell Proliferation, Differentiation and Function in a Bioreversible Manner*, 4 CLINICAL CASES IN MINERAL AND BONE METABOLISM 146 (2007) ("bisphosphonates can be divided into two groups with distinct molecular mechanisms of action ….The nitrogen-containing bisphosphonates act on osteoclasts … while non-nitrogen-containing bisphosphonates, like clodronate … induce[] inhibition of the ADP/ATP translocase") (Ex. 42).

[58] 5/18/2007 Dep. of Robert Marx, D.D.S. at 680, *In re Aredia® & Zometa® Prods. Liab. Litig.*, 3:06-MD-1760 (M.D. Tenn.) (Ex. 43).

[59] Plaintiffs may contend that Gotcher & Jee is relevant because a Novartis scientist, Jonathan Green, testified that he first became aware of the existence of this study in early 1986. Dr. Green, however, did not connect Gotcher & Jee to ONJ at that time. He had no basis to do so, given that no other publications in the medical/scientific literature stated (or even suggested) that the findings in this rat study involving the non-nitrogen bisphosphonate clodronate meant that ONJ in humans was a possible side effect of the nitrogen-containing bisphosphonates Aredia and Zometa.

[60] *See* Trial Tr. at 102-04, *Chiles v. Novartis Pharm. Corp.*, No. 3:06-cv-96-J-25JBT (M.D. Fla. Feb. 13, 2013) (excluding Gotcher & Jee article) (Ex. 45); Trial Tr. at 34-42, *Davids v. Novartis Pharm. Corp.*, 2:06-cv-0431-ADS (E.D.N.Y. Oct. 3, 2012) ("*Davids* 10/3/12 Tr.") (same) (Ex. 46).

jaw" is irrelevant, would only serve to mislead and confuse the jury, and should be excluded under Rules 401-03.[61]

C. The unrelated genetic disease osteopetrosis is irrelevant.

Osteopetrosis is a genetic disorder that profoundly affects the entire skeletal system and causes a variety of other serious medical conditions, including an inability to fight infection. It causes deformities of the skull and scoliosis of the spine, loss of hearing and sight, fragile bones prone to injury, and a host of other problems throughout the body.[62] Often, patients with osteopetrosis do not even live to adulthood. Because osteopetrosis typically impairs the normal functioning of osteoclasts, because Aredia and Zometa also inhibit osteoclasts (though by a different mechanism), and because some types of osteopetrosis bring about osteomyelitis of the jaw, plaintiffs contend that Novartis should have known that Aredia and Zometa could cause ONJ. The issue of osteopetrosis should be excluded because it is irrelevant. ONJ is not osteopetrosis and is not a genetic disease. The patients with osteopetrosis described in the medical literature were not receiving Aredia or Zometa or any other bisphosphonate drug. To the extent there is any relevance, evidence and argument regarding osteopetrosis still should be excluded as yet another convoluted example bound to confuse and mislead any jury.[63]

D. Potential ONJ cases in clinical trials patients were identified retrospectively and should be excluded under Rule 407.

Plaintiffs likely will also point to six suspected cases of ONJ in patients participating in the Aredia or Zometa clinical trials as "notice" that these drugs could cause ONJ. First, plaintiffs have no qualified expert who can discuss the design of the clinical trials and whether any clinical trial

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[61] *See* 1/12/2012 Trial Tr. at 69-70, *Kyle v. Novartis Pharm. Corp.*, 1:06-CV-00035 (W.D. Ky.) (excluding phossy jaw) (Ex. 48); *In re Fosamax Prod. Liab. Litig.*, 645 F. Supp. 2d 164, 198 (S.D.N.Y. 2009) (excluding same opinions under Fed. R. Evid. 403).

[62] *See* Expert Report of Dr. Serge Ferrari, MD at 7-8, 10 (Ex. 49).

[63] *See* Fed. R. Evid. 403, 703; *Davids* 10/3/12 Tr. at 41-42 (excluding testimony on osteopetrosis).

patient actually had ONJ.[64] Second, the six potential cases of ONJ were identified as part of a review Novartis conducted of its clinical trials databases in March 2005 to search for any symptoms that could be consistent with ONJ, in an effort to ensure that Novartis could make more accurate statements concerning ONJ and improve the label for future users.[65] This retrospective analysis, which occurred years after Mr. Earp's precipitating extractions in 1999 and 2001 and over a year after his last bisphosphonate use, in January 2004, is the essence of a subsequent remedial measure and should be excluded under Federal Rule of Evidence 407.

III. The Court Should Exclude Preempted Arguments About Labeling And Dosing Issues Controlled By the FDA.

The Court should exclude evidence and argument that Novartis should have altered the FDA-approved prescribing information for its prescription drugs Aredia and Zometa by: (1) recommending dosing less frequently than the 3-4 week dosing interval approved by FDA or that treatment be halted after a certain period of time; (2) adding a "black box" warning regarding the risk of ONJ; or (3) using different label formatting (*e.g.*, placing the warning regarding ONJ in a different section of the label or using a different font size or bolded text). These claims are preempted by federal law.[66]

A. Plaintiffs' suggested label changes on dosing and duration of use are preempted.

Novartis expects that plaintiffs will argue that Novartis should have (1) recommended less frequent dosing than the 3-4 week Aredia and Zometa dosing intervals approved by FDA, and (2)

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[64] *See* 9/11/2013 Order at 6, D.E. 100 (precluding Dr. Marx from "criticiz[ing] Novartis's clinical trials or opin[ing] on patients in those trials).

[65] *See* March 2005 Oncologic Drugs Advisory Committee Background Information at 22 (ZA-0702841-976) (Ex. 50).

[66] *See PLIVA, Inc. v. Mensing*, 131 S. Ct. 2567 (2011) (federal law preempts claims that a drug company should have given a warning if the company could not add it to the label without FDA approval); *Mutual Pharm. Co. v. Bartlett*, 133 S. Ct. 2466 (2013) (indicating that *PLIVA* preemption reasoning applies to both generic and brand name prescription drugs).

suggested ceasing Aredia or Zometa after a certain number of doses or months of treatment.[67] Because Novartis could not have made the recommendations plaintiffs advocate without prior FDA approval, such claims are preempted under the authority of the Supreme Court's holdings in *Mensing* and *Bartlett*.

In *Bartlett*, the Supreme Court made clear that federal law prohibits an independent change to dosing or duration whether by a generic *or a brand name* drug manufacturer:

> Once a drug – whether generic *or brand-name* – is approved, the manufacturer is prohibited from making any major changes to the "qualitative or quantitative formulation of the drug product, including active ingredients, or in the specifications provided in the approved application."[68]

The Court made this statement immediately after setting forth the factors that go into the drug's "formulation," including "dosage form, strength . . . [and] rate and extent of absorption."[69] *Bartlett* then makes clear that any changes in the dose or duration of a drug would render the drug a "new drug" requiring new approval by FDA: "[T]he FDCA requires a generic drug to have the same active ingredients, route of administration, dosage form, strength, and labeling as the brand-name drug on which it is based. [W]ere Mutual to change the composition of sulindac, the altered chemical would be a new drug that would require its own NDA to be marketed in interstate commerce."[70] In reaching this conclusion, the Court relied in part on 21 C.F.R. § 310.3(h)(5), which directs FDA to consider a drug to be a new drug when its label is changed to indicate "newness of a *dosage*, or method or *duration of administration or application*, or other condition of use prescribed, recommended, or

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[67] *See, e.g.*, Expert Report of James M. Vogel, M.D. ("Vogel Report") ¶¶ 58-59 ("Consideration should be directed as to whether a change in schedule can also reduce the incidence of ONJ."); *id*. ¶¶ 56-57 ("It is reasonable to ask whether an alteration in the duration . . . of treatment with intravenous bisphosphonates would produce an acceptable benefit without increasing risk.") (D.E. 73-1); 6/12/13 *Hill* Trial Tr. at 552 (Dr. Marx claims that risks of Zometa outweigh its benefits "after 10 doses") (Ex. 51).

[68] *Bartlett*, 133 S. Ct. at 2471 (quoting 21 C.F.R. § 314.70(b)(2)(1)).

[69] *Id.* A drug's composition includes its dosage form and strength. *Id.* Any change to the composition of a drug requires prior FDA approval via the New Drug Application process. *Id.*

[70] *Id.* at 2475.

suggested in the labeling of such drug, even though such drug when used in other dosage, or other method or duration of administration or application, or different condition, is not a new drug.."[71]

This ruling affirmed and clarified the Supreme Court's holding in *Mensing*, in which the Court determined that the preemptive effect of federal drug regulations turned on "whether the private party could *independently* do under federal law what state law requires of it."[72] There are many label changes that Novartis *cannot* make unilaterally: prior FDA approval is required for any change that "has a substantial potential to have an adverse effect on the identity, strength, quality, purity or potency of the drug product as these factors may relate to the safety or effectiveness of the drug product."[73] A labeling change that recommended reduced dosing of Aredia or Zometa as compared to the 3-4 week interval dosing schedule with no specified cutoff that FDA approved would have a direct adverse effect on the strength and potency of the drug product as prescribed and could undermine the efficacy of the treatment. Any label change to the dosing interval or duration would have been a major change under § 314.70(b) that would have required prior approval.[74] According to *Mensing*, "when a party cannot satisfy its state duties without the Federal Government's special permission and assistance, which is dependent on the exercise of judgment by a federal agency, that party cannot independently satisfy those state duties for preemption

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[71] 21 C.F.R. § 310.3(h)(5) (emphasis added); *see Bartlett*, 133 S. Ct. at 2475. The amount and timing of a prescription drug's dose is determined in dosing studies, which are extensively regulated by FDA. Dosing information must be based upon "adequate and well-controlled studies." 21 C.F.R. § 314.126. And *changing* a dosing regimen, or adding one to the label, requires new clinical trials. *See* http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm111354.htm ("When FDA approves a drug, the labeling includes information on benefits and risks and the appropriate dosing regimens," and "to change or add a new dosing regimen to the labeling, the sponsor must submit data to FDA from clinical trials that show the new regimen is safe and effective.") (Ex. 52) But no trials have been done that justify a change in the Aredia or Zometa dosing regimen.

[72] *Mensing*, 131 S. Ct. at 2579 (emphasis added).

[73] 21 C.F.R. § 314.70(b).

[74] *See Bober v. Glaxo Wellcome PLC*, 246 F.3d 934, 942 (7th Cir. 2001) (holding that drug company could not "recommend or even suggest" use of a drug at dosage level not approved for such purpose by FDA).

purposes."[75] Because Novartis could not recommend, without prior FDA approval, the alternative dosing regimen that plaintiffs may claim was required under state law, that theory of liability is preempted under *Mensing* and *Bartlett*. Accordingly, testimony and argument addressed to those claims should be excluded as irrelevant, confusing, misleading, and unduly prejudicial under Rules 401-03.

B. Plaintiffs are preempted from suggesting that Novartis could have added a "black box" warning to its Aredia or Zometa labels.

In recent Aredia/Zometa trials, plaintiffs' counsel have suggested to the jury that Novartis failed to provide adequate warnings because it did not add what is known as a "black box" warning to the Zometa label.[76] Not only do plaintiffs lack evidentiary support that FDA would approve of a black box ONJ warning for Aredia or Zometa, which it has never required, but FDA regulations prohibit Novartis from including a black box warning without FDA's prior approval.[77]

FDA has retained exclusive control over the decision as to whether and when a black box warning may be added because "[t]he intent of the box is to draw special attention to the warning" and it exercises "restraint in requiring warnings to be boxed because overuse of the box will ultimately lead to reducing its effect."[78] The FDA's consistently expressed position that a

[75] *Mensing*, 131 S. Ct. at 2580-81.

[76] A black box or boxed warning is a bolded statement with the heading "WARNING" and appears at the beginning of the label within a black box. *See* 21 C.F.R. § 201.57(a)(4), (c)(1). *See, e.g.*, 4/2/12 Trial Tr. in *Winter ex rel. Baldwin v. Novartis Pharm. Corp.*, No. 2:06-cv-04049 (W.D. Mo.) at 1766 ("4/2/12 *Winter* Trial Tr.") (plaintiff's counsel's examination of Dr. Arrowsmith: "Q. Did Novartis ever consider putting a black box warning on Zometa? A. Not that I'm aware of, no."); *id.* at 1767 (plaintiff's counsel asserting, "if they had decided to get people's attention, they could have requested that the FDA approve a label with a black box warning") (Ex. 53).

[77] *See* 44 Fed. Reg. 37434, 37448 (June 26, 1979) ("The Commissioner advises that, to ensure the significance of boxed warnings in drug labeling, they are permitted in labeling only when specifically required by the FDA.").

[78] 51 Fed. Reg. 43900-01, 43902 (Dec. 5, 1986); *see also* 4/2/12 *Winter* Trial Tr. at 1768 ("FDA has made it very clear that they use black box warnings very carefully. They don't want to overuse black box warnings because then people don't notice them at all.").

manufacturer cannot unilaterally add a black box warning controls here.[79]

Because the FDA prohibits black box warnings absent prior FDA approval, Novartis could not unilaterally include a boxed warning in the Aredia or Zometa label. Under *Mensing* and *Bartlett*, any claim that Novartis should have included a black box warning in the Aredia or Zometa label is preempted.[80]

The Supreme Court's earlier opinion in *Wyeth v. Levine* is not to the contrary. In *Levine*, the Supreme Court ruled that a plaintiff's failure to warn claim was not preempted because it could have used the CBE process to make the particular label change at issue in that case.[81] The *Mensing* Court explained that its holding was consistent with *Levine* because in *Levine* "The Court . . . asked what the drug manufacturer could independently do under federal law . . . . But here, 'existing' federal law directly conflicts with state law."[82] What the Court found that Wyeth could do independently under federal law was make unilateral CBE changes, and not any of the types of changes addressed by this motion. For the changes at issue here, which require prior FDA approval, *Mensing* and *Bartlett* govern.

C. Arguing for different label formatting is preempted.

Plaintiffs likely will argue that Novartis should have formatted the Aredia and Zometa labels

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[79] *See Mensing*, 131 S. Ct. at 2575 ("The FDA's views are controlling unless plainly erroneous or inconsistent with the regulation[s] or there is any other reason to doubt that they reflect the FDA's fair and considered judgment." (quotations omitted)).

[80] *See Mensing*, 131 S. Ct. at 2580 ("[P]re-emption analysis should not involve speculation about ways in which federal agency and third-party actions could potentially reconcile federal duties with conflicting state duties. When the 'ordinary meaning' of federal law blocks a private party from independently accomplishing what state law requires, that party has established pre-emption."); *see also Dopson-Troutt v. Novartis Pharm. Corp.*, No. 8:06-cv-1708, 2013 WL 5330463, at *6-9 (M.D. Fla. Sept. 23, 2013) (holding, in Aredia/Zometa case, claim that Novartis should have added a black box warning preempted under *Bartlett/Mensing* rationale).

[81] *Wyeth v. Levine*, 129 S. Ct. 1187, 1196 (2009) ("There is, however, an FDA regulation that permits a manufacturer to make *certain changes* to its label before receiving the agency's approval." (emphasis added)).

[82] *Mensing*, 131 S. Ct. at 2581 n.8.

differently by, among other things, placing the ONJ warning in a section of the label other than the adverse reactions section or using a different font or bolded text. For example, in a recent trial, plaintiff's counsel brandished the actual Zometa label and put it in evidence so jurors could scrutinize, not its content, but the placement of its folds.[83] Such argument is preempted because FDA comprehensively regulates the formatting of prescription drug labeling.[84]

IV. Evidence Or Argument That Novartis Had A Duty to Warn Anyone Other Than Mr. Earp's Prescribing Physicians Is Irrelevant and Unduly Prejudicial Because It Suggests An Incorrect Legal Standard and Does Not Fit The Facts Of This Case.

Plaintiffs likely will attempt to argue and introduce evidence to the effect that Novartis had a duty to warn Mr. Earp's dentists, oral surgeons, and other medical providers of the alleged connection between Novartis's drugs and ONJ. Any such argument or evidence would contradict North Carolina law, which imposes a duty for drug manufacturers to warn *solely* the patient's prescribing physician, and thus it is irrelevant and inadmissible under Rules 401-03. It also is irrelevant because plaintiffs have no evidence that a different warning to any of Mr. Earp's dentists or oral surgeons could have affected the course of his alleged injury.

North Carolina law is clear that Novartis's duty to warn extends only to the prescribing physician. Pursuant to N.C. Gen. Stat. § 99B-5(c), if a drug manufacturer provides an adequate warning "to the physician or other legally authorized person *who prescribes or dispenses that*

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[83] *See* 2/11/13 Pl.'s Opening Statement at 140-41, *Chiles v. Novartis Pharm. Corp.*, No. 3:06-cv-96-J-25JBT (M.D. Fla.) ("This is a package insert that's attached to one of these marketing things. *Here's a little package insert.* So rather than putting something under the warning section, *it went to the back,* . . . ." (emphasis added)) ("*Chiles* 2/11/13 Tr.") (Ex. 54).

[84] *See, e.g.*, 21 C.F.R. § 201.57(d) (setting forth formatting requirements for drug labels); *see also Pom Wonderful LLC v. Coca-Cola Co.*, 679 F.3d 1170, 1177-78 (9th Cir. 2012) (concluding that the plaintiff's claim that defendant should have "alter[ed] the size of the words on its labeling" invades the province of FDA and would "undermine the FDA's regulations and expert judgments"). In addition, plaintiffs have no admissible expert testimony on the adequacy of the Aredia or Zometa labels. *See* 9/11/2013 Order at 6, D.E. 100 (preventing Drs. Skubitz and Vogel from discussing "labeling" and precluding Dr. Parisian from opining on "whether the labels provided adequate warnings in this case"). Absent such testimony, any argument or evidence regarding the format of the labeling cannot reliably be tied to this case and would be irrelevant, confusing, and unfairly prejudicial to Novartis. Fed. R. Evid. 401-03.

prescription drug for the claimant," the manufacturer cannot be liable for failure to warn.[85] This statute codifies the learned intermediary doctrine, under which "the manufacturer's duty to warn *extends only to the prescribing physician*, who then assumes responsibility for advising the individual patient of risks associated with the drug or device."[86] Statements suggesting that Novartis had a duty to warn other treating but not prescribing health care providers are irrelevant to any actual or disputed issue in this case and would be profoundly prejudicial as they would encourage the jury to apply the wrong legal standard.[87]

In another Aredia/Zometa case, this Court acknowledged that the proper statement of the law with respect to § 99B-5(c) focuses on the prescribing physician, stating that "[t]he unambiguous language of § 99B-5(c) provides that if a pharmaceutical company gives adequate warning to claimant's prescribing physician, the manufacturer shall not be liable for failing to provide warning directly to the claimant . . . ."[88] Although the *Brown* court initially denied Novartis's motion to exclude evidence regarding warnings to warn to anyone other than the prescribing physician, it planned to "revisit this argument" at trial.[89] It did not have an opportunity to do so, because the

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[85] N.C. Gen. Stat. § 99B-5(c) (West) (emphasis added). An exception exists when the FDA requires a "direct consumer warning or instruction to accompany the product," *id.*, but that is not the case here.

[86] *Odom v. G.D. Searle & Co.*, 979 F.2d 1001, 1003 (4th Cir. 1992) (emphasis added); *see also Cowley v. Abbott Labs., Inc.*, 476 F. Supp. 2d 1053, 1060 (W.D. Wis. 2007) (observing that North Carolina codified the learned intermediary doctrine in N.C. Gen. Stat. Ann. § 99B-5); *Baraukas v. Danek Med., Inc.*, No. 6:97CV00613, 2000 WL 223508, at *4 (M.D.N.C. Jan. 13, 2000) (noting that North Carolina courts have "adhere[d] to the learned intermediary doctrine," under which a manufacturer of a drug "dispensed to patients by doctors . . . has a duty to warn only the doctor, rather than the patients of any risks associated with the product's use. It is assumed that the doctors will pass along appropriate information to their patients.") (Ex. 22); *Talley v. Danek Med., Inc.*, 7 F. Supp. 2d 725, 730 (E.D. Va. 1998) (observing that for medical devices that are available only through prescription, the duty to warn under the learned intermediary doctrine is limited to the prescribing doctor).

[87] *Cf. Furka v. Great Lakes Dredge & Dock Co.*, 755 F.2d 1085, 1089 (4th Cir. 1985) (reversible error occurs where jury instruction misstates "fundamentally controlling substantive principles" of law, even in the absence of objection); *Miller v. Premier Corp.*, 608 F.2d 973, 983 (4th Cir. 1979) (same).

[88] *Brown v. Novartis Pharm. Corp.*, No. 7:08-cv-130-FL, 2012 WL 3066588, at *11 (E.D.N.C. Jul. 27, 2012).

[89] *Id.* at *12.

plaintiff dismissed the case on the third day of trial.[90] In any case, if § 99B-5(c) is accepted as the correct legal standard, then it follows that any evidence to support any other legal arguments is irrelevant and inadmissible.[91]

Plaintiffs likely will point to rulings in *Fussman v. Novartis Pharmaceuticals Corp.* to support the contention that failure to warn Mr. Earp's dental professionals is relevant to proximate cause in this case. *Fussman*, however, was based in part on a North Carolina case, *Holley v. Burroughs Wellcome Co.*, decided a decade before § 99B-5 was codified, and whose facts are inapposite to those here.[92] In *Holley*, decided on a summary judgment and not an evidentiary standard, the North Carolina Supreme Court focused on how the drug manufacturer's warnings may have affected the care provided by the anesthesiologist and nurse who prescribed and administered the manufacturer's product.[93] This is made clear in the underlying decision, where the North Carolina court of appeals pointedly only extended the duty to warn to "other health care professionals *using* the products."[94] In this case, Mr. Earp's dentists and oral surgeons were not users of Novartis's products, foreseeable or otherwise. Because of the learned intermediary doctrine embodied in North Carolina law, only Mr. Earp's prescribing oncologists, Drs. Kritz and Yoffe, were foreseeable users of Aredia and Zometa. Novartis's duty to warn extends solely to them, and therefore only evidence

[90] *Brown v. Novartis Pharm. Corp.*, No. 7:08-cv-130-FL, Trial Tr. at 3 (E.D.N.C. Sep. 21, 2012) (Ex. 55).

[91] Fed. R. Evid. 401-03; *see also United States v. Jefferson*, 623 F. Supp. 2d 678, 680-81 (E.D. Va. 2009) (excluding under Fed. R. Evid. 402 irrelevant standards of conduct in criminal prosecution).

[92] *See Fussman v. Novartis Pharm. Corp.*, 106CV149, 2010 WL 4104707, at *2 (M.D.N.C. Oct. 18, 2010).

[93] *See Holley v. Burroughs Wellcome Co.*, 318 N.C. 352, 353-54, 348 S.E.2d 772, 773 (1986) (noting that plaintiff's symptoms were not recognized "either by Dr. Hooper or Nurse Evans, and thus not properly treated in time to prevent injury").

[94] *Holley v. Burroughs Wellcome Co.*, 74 N.C. App. 736, 746-47, 330 S.E.2d 228, 235 (1985) (emphasis added; noting that the nurse who induced and maintained the anesthesia in question was "a foreseeable user of defendants' products to whom defendants' duty to warn applied"), *aff'd*, 318 N.C. 352, 348 S.E.2d 772 (1986).

of Novartis's warnings to Mr. Earp's prescribing physicians is relevant and admissible under Rules 401-403.

Evidence or argument regarding how different warnings may have changed the practices of Mr. Earp's dentists or oral surgeons is also irrelevant because plaintiffs have no evidence that such a warning would have mattered in this case. Plaintiffs may argue that Dr. Earp's dentist Dr. Petrocella and oral surgeon Dr. Davis would have acted differently given a different warning.[95] However, neither dentist specified what such a change would be, making such a contention mere speculation.[96] Plaintiffs also have no evidence that any treatment by Drs. Petrocella or Davis could have been avoided.[97] In addition, Mr. Earp's allegedly precipitating extractions, in 1999 and 2001, and Dr. Davis' last active treatment for Mr. Earp, in early 2002,[98] all occurred well before Novartis received its first adverse event report regarding ONJ, in December 2002.[99] By the time Novartis and the medical world were first learning about reports of ONJ in bisphosphonate users, it was too late for

[95] *See* Pls.' Opp. to Def.'s 2d Mot. for Summ. J., D.E. 81, at 10 (Dr. Petrocella "had no knowledge of the increased risk of jawbone death at the time he extracted Mr. Earp's teeth so he did not factor that into his decision making differential"), 13 (Dr. Davis "testified that if he had been aware" of the potential complications from tooth extractions and debridements with Aredia and Zometa, "he would have changed how he treated Mr. Earp"). Both of Mr. Earp's oncologists, however, testified that, knowing what they know now, they still would have prescribed Aredia for Mr. Earp. *See* Yoffe Dep. at 91-92; Kritz Dep. at 64-65. Plaintiffs therefore cannot meet their burden of proof on warnings causation. *See Luttrell v. Novartis Pharm. Corp.*, No. 12-35893, 2014 WL 644880, at *1 (9th Cir. Feb. 20, 2014) (affirming summary judgment in Aredia/Zometa case because plaintiff could not prove proximate cause when it was clear his doctor would not have changed his prescribing decision).

[96] *See, e.g., Dunn v. Sandoz Pharm. Corp.*, 275 F. Supp. 2d 672, 684 (M.D.N.C. 2003) ("Ultimately, speculation is unreliable evidence and is inadmissible."); *cf. Fussman v. Novartis Pharm. Corp.*, No. 1:06-cv-149, 2011 WL 5836928, at *3 (M.D.N.C. Nov. 21, 2011) (noting that plaintiff's "treating dentists and oral surgeons all testified to various ways they would have changed their treatment of her had an adequate warning been provided.").

[97] *See, e.g., Zimmerman v. Novartis Pharm. Corp.*, 287 F.R.D. 357, 361 (D. Md. 2012) (granting summary judgment in Aredia/Zometa case where plaintiff could not prove that a different warning would have changed her dental treatment).

[98] *See* Dep. Tr. of Steven H. Davis, DDS at 76-79 (testifying he referred Mr. Earp for other treatment after last seeing him February 2002) (Ex. 56).

[99] The extraction of Mr. Earp's tooth #12 also occurred prior to Novartis's first adverse event report, in August 2002. *See* Health Care Record of 8/7/2002 (11212-0011) (Ex. 57).

any warning to Mr. Earp's dental professionals to have made any difference. Evidence or argument about the lack of a warning to Mr. Earp's dental care providers is simply irrelevant, may only serve to mislead and confuse the jury, and should be excluded under Rules 401-03.

V. Miscellaneous Motions In Limine

a. The Court should exclude medical costs for Mr. Earp's Aredia and Zometa infusions, which were not proximately caused by his alleged injury. Plaintiffs seek to recover $240,570.91 in medical expenses, over half of which ($141,128) is for the cost of the Aredia and Zometa infusions which Mr. Earp received as part of his treatment for multiple myeloma.[100] A "[p]laintiff is, of course, entitled to damages only if they are the natural and proximate result of defendant's negligence."[101] Even assuming that Aredia or Zometa did cause Mr. Earp's jaw injury (which Novartis denies), those infusions were not proximately caused by any alleged negligence or wrongdoing by Novartis.[102] The "injury" that proximately caused Mr. Earp (or someone on his behalf) to pay for Aredia and Zometa infusions was the multiple myeloma that "certainly" put him at risk for skeletal problems.[103] Other courts in the Aredia/Zometa litigation have precluded plaintiffs from seeking the costs of their infusions.[104] This Court should do the same.[105]

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[100] *See* Pls.' Resp. to Novartis's First Set of MDL Interrogs., Resp. to Interrog. 4 & Ex. A (listing "all fees and charges attributable to Defendant") (Ex. 58).

[101] *Taylor v. Boger*, 289 N.C. 560, 568, 223 S.E.2d 350, 355 (1976).

[102] In addition, plaintiffs have not shown that the cost of Mr. Earp's infusions from April 2002 forward ($47,863), a time when plaintiffs cannot prove that Mr. Earp was being treated with a Novartis drug, is "attributable to Defendant." *See supra*, Novartis's MIL No. 1.

[103] Kritz Dep. at 60. In addition, any "damage" attributed to Mr. Earp's infusions would have to be offset by the benefit they provided to him. *See* Yoffe Dep. at 87-88 (testifying that, until he put them on hold in 2004, bisphosphonates were continuing to provide benefits to Mr. Earp); *id.* at 129 (Mr. Earp is "kind of a walking miracle").

[104] *See* Order, *Meng v. Novartis Pharm. Corp.*, No. MID-L-7670-07-MT (N.J. Super. Ct. Aug. 8, 2012) (precluding plaintiff from seeking costs of Zometa infusions as damages) (Ex. 59); *Davids* 11/1/12 Tr. at 2812-15 (declining plaintiff's proposed jury instruction on cost of Zometa infusions because Zometa was prescribed for plaintiff's underlying cancer and not as a consequence of plaintiff's alleged ONJ).

[105] Plaintiffs likely will note that the cost of Aredia/Zometa infusions was allowed at the *Fussman* trial. *See* Trial Tr. at 22:3-23:14, *Fussman v. Novartis Pharm. Corp.* (M.D.N.C. Nov. 10, 2010). There, the

b. The Court should exclude photographs of injuries in patients other than Mr. Earp under Fed. R. Evid. 401-03. Plaintiffs may seek to introduce photographs of other persons who have ONJ, have other jaw disorders, or have undergone dental surgery. These photographs may come from textbooks or the patient files of plaintiffs' experts. They do not depict the injuries experienced by Mr. Earp, and such photographs are irrelevant to the condition of his mouth and jaw during the periods of time that he experienced jaw problems. These photographs would very likely prejudice the jury, which may find it difficult to separate Mr. Earp's actual condition from the very graphic photographs of other patients who may have presented with different cancer forms and diseases and more severe jaw problems than Mr. Earp experienced. The potential prejudicial effect of such photographs greatly outweighs their probative value and they should be excluded under Rules 401-03.[106]

c. The Court should exclude sales and marketing materials that were neither seen nor relied upon by Mr. Earp's prescribing physicians. Plaintiffs may try to introduce evidence relating to Novartis marketing and promotional activities that were directed to the attention of prescribing physicians and patients.[107] Plaintiffs should not be permitted to introduce such evidence

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trial court mistakenly believed that the costs should be included because of Mrs. Fussman's "sworn statement" that she would not have taken the drug if warned. Here, Mr. Earp has made no such statement, and any new statement to that effect should be excluded. *See infra* Novartis's MIL No. V.d.

[106] *See Edwards v. ATRO SpA*, 891 F. Supp. 1074, 1084 (E.D.N.C. 1995) (excluding evidence of products other than the specific nail gun in question, because "the probative value of introducing such other tools is outweighed by unfair prejudice and danger of misleading the jury"); *see also United States v. Myers*, 280 F.3d 407, 414 (4th Cir. 2002) (approving of attempt to minimize prejudice to plaintiff by excluding inflammatory photographs).

[107] *See Chiles* 2/11/13 Tr. ("[Novartis] did a marketing meeting, and they came up with the Zometa strategy."), *id.* at 138 ("[y]ou will also see pamphlets . . . that they give to oncologists to give to patients"), *id.* at 139 ("you'll see . . . the Journal of Clinical Oncology, advertising for Zometa"); 3/2004 Journal of Clinical Oncology Zometa® advertisement (Ex. 60); Zometa® pamphlet (ZAEM-00958409-12) (Ex. 61).

because they cannot establish that it was seen and relied upon by Mr. Earp's prescribing physicians, Dr. Kritz or Dr. Yoffe.[108]

d. The Court should exclude statements by Mr. Earp that he would not have used Aredia or Zometa if he had been told about the risk of ONJ. Novartis expects that Mr. Earp will claim at trial, for the first time, that he would not have taken Aredia or Zometa if he had been warned of the alleged association between Aredia and Zometa and ONJ. Mr. Earp's claims (and statements of any other witnesses to this effect) are irrelevant, because the relevant inquiry under North Carolina's learned intermediary doctrine is whether Mr. Earp's prescribing physicians would have prescribed Aredia and Zometa to him, not whether he would have taken the drugs if his physicians had been warned.[109] Statements regarding whether Mr. Earp would not have taken Aredia or Zometa had he been warned about ONJ in 1998 are also inadmissible because they are "self-serving opinions without objective corroboration" and therefore are "not significantly probative."[110]

e. The Court should exclude references to Reclast and other Novartis drugs which are not at issue in this case. Novartis expects that plaintiffs will attempt to argue that Novartis delayed its warning on the alleged association between bisphosphonates and ONJ because of, in part, a desire to keep the warning off the Reclast[111] label, an osteoporosis medication.[112] Any argument or

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[108] *See* Fed. R. Evid. 401-02; *see also, e.g., In re Seroquel Prod. Liab. Litig.*, No. 6:06-md-1769-Orl-22DAB, 2009 WL 223140, at *4-5 (M.D. Fla. Jan. 30, 2009) (promotional material excluded in the absence of connection with prescribing physician); *In re Norplant Contraceptive Prod. Liab. Litig.*, MDL 1038, 1997 WL 81092, at *1 (E.D. Tex. Feb. 21, 1997) (same) (Ex. 70).

[109] *See* N.C. Gen. Stat. Ann. § 99B-5(c) (focusing on the warning given to the prescribing physician, not the patient).

[110] *Evans v. Technologies Applications & Serv. Co.*, 80 F.3d 954, 962 (4th Cir. 1996) (upholding decision to strike and disregard Title VII plaintiff's self-serving assertions).

[111] Reclast has a base molecule of zoledronic acid, like Zometa. Reclast, however, is dosed in a different amount, is administered on a different schedule, is indicated for treatment of bony issues in patients without cancer, and is treated as a different drug by the FDA. *See* Reclast Label (Ex. 62).

[112] *See* Mot. Hr'g at 40, *Davids v. Novartis Pharm. Corp.*, No. 2:06-cv-0431-ADS (E.D.N.Y. July 9, 2012) (Ex. 63); Mot. Hr'g at 72-73, *Winter v. Novartis Pharm. Corp.*, No. 2:06-cv-4049-MJW (W.D. Mo. Feb. 29, 2012) (Ex. 64).

evidence relating to other FDA-regulated Novartis medications, including Reclast, is irrelevant to the central question in this case: whether Novartis's warnings regarding Aredia and Zometa were adequate.[113] Such evidence also "would cause Novartis unfair prejudice and potentially confuse the jury."[114] This Court should exclude references to Reclast and other Novartis drugs under Rules 401-03.

f. The Court should exclude evidence of ADE reports received by Novartis because plaintiffs cannot prove that they are substantially similar to the alleged event in this case.

Plaintiffs may seek to offer evidence of ADE reports from 1996 and 1998 as evidence of "notice." These two anecdotal reports, which do not state that the patient has ONJ as opposed to any number of other potential jaw maladies, are irrelevant, Rule 401-02, and any probative value is substantially outweighed by the risk of confusing and misleading the jury, Rule 403.[115]

March 14, 2014

Respectfully submitted,

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[113] *See Kyle*, 835 F. Supp. 2d at 319 (excluding, in Aredia/Zometa case, evidence related to any other of Novartis's drugs, including Reclast, as "irrelevant to the instant matter.")

[114] *Id.*

[115] *See Renfro Hosiery Mills Co. v. Nat'l Cash Register Co.*, 552 F. 2d 1061, 1068-69 (4th Cir. 1977) (upholding exclusion of data and reports under Rule 403 because the evidence was not "substantially similar" and because the "particular evidence proffered was voluminous and complex" with "little if any probative value but rather considerable potential for prolongation of the trial and possible confusion of the issues").

CERTIFICATE OF SERVICE

I hereby certify that I electronically filed the foregoing Novartis Pharmaceuticals Corporation's Memorandum in Support of Omnibus Motion *in Limine* via the CM/ECF system, which will send notification of such filing to CM/ECF participants:

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This the 14th day of March, 2014.

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